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| EXAMINER |
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ROYDS, LESLIE A

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1614

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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|------------------------------|--------------------------------------|---|--|
| Office Action Summary | Application No. 10/626,037 | Applicant(s) SCHERER, WARREN J. | |
| | Examiner Leslie A. Royds | Art Unit 1614 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period **will** apply and **will** expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply **will**, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 February 2008 and 28 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,11,12 and 34-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-2,11-12,34-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>21 February 2008</u> . | 6) <input type="checkbox"/> Other: _____. |

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DETAILED ACTION

Claims 1-2, 11-12 and 34-36 are presented for examination.

Applicant's Amendment filed February 21, 2008 and Supplemental Amendment filed February 28, 2008 have each been received and entered into the present application.

Applicant's Information Disclosure Statement (IDS) filed February 21, 2008 has been received and entered into the present application. As reflected by the attached, completed copy of form PTO/SB/08a (two pages total), the Examiner has considered the cited references.

Claims 1-2, 11-12 and 34-36 are pending and under examination. Claims 3-4, 7-10, 14-17, 19-25 and 27-33 are cancelled, claims 34-36 are newly added and claims 1-2 are amended.

Applicant's arguments, filed February 21, 2008 and February 28, 2008, have been fully considered. Rejections and objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description Requirement

(New Grounds of Rejection)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 36 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Present claim 36 is directed to a method of treating facial flushing associated with menopause-

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associated hot flashes in a human in need thereof, the method comprising topically administering a composition comprising an effective amount of brimonidine tartrate and a dermatologically acceptable carrier.

In particular, the specification and claims as originally filed fail to provide adequate written description for the newly added limitations directed to the application of an effective amount of brimonidine tartrate and a dermatologically acceptable carrier to the site of the facial flushing on the human (claim 36).

MPEP §2163 states, “The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, “does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.” *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test of sufficiency of support in a parent application is whether the disclosure of the application relied upon “reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter.” *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983))...Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991).”

Applicant discloses at p.5, l.24-p.6, l.2, "For the treatment of facial flushing in humans, one

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embodiment of the subject invention provides a (2-imidazolin-2-ylamino) quinoxaline derivative, such as brimonidine tartrate admixed with a dermatologically acceptable carrier which is then administered topically in accordance with the present invention to skin. Any suitable, conventional, dermatologically acceptable carrier may be employed. A carrier is dermatologically acceptable if it does not inhibit the effectiveness of the active compound(s) and it has substantially no long term or permanent detrimental effect on the skin to which it is administered. In various preferred embodiments, compositions of the subject invention are topically administered to facial skin.”

However, such disclosure of the application of brimonidine tartrate topically to the skin or, preferably, to facial skin, fails to provide adequate written support to now claim the same topical application of brimonidine tartrate specifically to the site of the facial flushing in the subject being treated. This is a clear narrowing of the subject matter both claimed and disclosed in the specification and claims as originally filed that is not adequately supported, either explicitly or implicitly, by the original disclosure. It is clear, therefore, that Applicant was not in possession of the concept of topical administration of brimonidine tartrate solely to the afflicted site of facial flushing, but rather was in possession of the concept of topically administering brimonidine tartrate to the skin (preferably the facial skin) *per se* as originally disclosed and claimed.

As stated in MPEP §2163, “The subject matter of the claim need not be described literally (i.e., using the same terms of *in haec verba*) in order for the disclosure to satisfy the description requirement.” However, considering the teachings provided in the specification as originally filed, Applicant has failed to provide the necessary teachings, by describing the claimed invention, in such a way as to reasonably convey to one skilled in the relevant art that Applicant had possession of the limitation directed to the application of an effective amount of brimonidine tartrate and a dermatologically acceptable carrier to the site of the facial flushing on the human (claim 36).

Accordingly, the claim is considered to lack sufficient written description and is properly rejected

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under 35 U.S.C. 112, first paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-2, 11-12 and 34-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wymenga et al. ("Management of Hot Flushes in Breast Cancer Patients", *Acta Oncologia*, 41(3), 2002; 269-275) in view of Gil et al. (U.S. Patent Application Publication No. 2003/0229088; Issued December 2003, Filed May 2002), and further in view of newly cited factual references to Burke et al. ("Preclinical Evaluation of Brimonidine", *Survey of Ophthalmology*, 41(Supp.1), 1996; S9-S18) and Dictionary.com ("Topical" and "Transdermal", 2008), each of record, for the reasons of record set forth at pages 12-15 of the previous Office Action dated August 21, 2007, of which said reasons are herein incorporated by reference, and further in view of the additional remarks:

Newly amended claim 1 and newly added claims 35-36 are properly included in the present rejection because Wymenga et al. teaches the treatment of menopausal symptoms, such as hot flashes, with clonidine, a centrally active alpha-adrenergic agonist that reduces vascular reactivity, in low dosages that were demonstrated to be effective in the reduction of hot flushes caused by normal menopause either when administered orally or transdermally (i.e., meets Applicant's newly added claim 35, which specifies administration to the skin of the human to be treated; abstract; col.2, para.2, p.269; col.2, para.4, p.271) and Gil et al. teaches other known alpha-adrenergic agonists, including, *inter alia*, clonidine, brimonidine, tizanidine, etc. (p.1, para.[0009]) and salts thereof, including the tartrate salt (p.13, para.[0091]), and

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compositions thereof (p.13, para.[0096]) in dermatologically acceptable formulations, such as, e.g., a dermal patch, topical drops, creams, gels or ointments, etc. (p.14, para.[0099]).

One of ordinary skill in the art would have found it *prima facie* obvious to use the brimonidine alpha-adrenergic agonist (or the tartrate salt thereof) as taught by Gil et al. for the treatment of menopausal hot flushes and the cutaneous flushing associated with the same because Gil et al. teaches such a compound as having potent activity in agonizing the alpha-adrenergic receptor and Wymenga et al. teaches significant reduction in the incidence of hot flushes in menopausal women when treated with an alpha-adrenergic agonist (i.e., clonidine) orally or transdermally. Such a person would have been motivated to do so because the brimonidine (or tartrate salt thereof) of Gil et al. was functionally equivalent for binding alpha-adrenergic receptor as the clonidine compound disclosed by Wymenga et al. for use in reducing the incidence of hot flushing in menopausal women. Thus, substituting the clonidine of Wymenga et al. with the brimonidine (tartrate) compound of Gil et al. would have been *prima facie* obvious and well within the purview of the skilled artisan because the same end result of agonizing the alpha-adrenergic receptors and thereby reducing menopausal hot flushes would have reasonably and predictably resulted, absent factual evidence to the contrary. Furthermore, the fact that Gil et al. confirms the amenability of brimonidine into a dermatologically acceptable formulation raises the reasonable expectation of success that the skilled artisan would have substituted the brimonidine compound of Gil et al. for the transdermal administration of clonidine as taught by Wymenga et al. because it was amenable to such a type of formulation and would have reasonably been expected to achieve the same, or at least substantially similar, reduction in the incidence of menopausal hot flushes and the cutaneous flushing associated therewith.

Though Gil et al. fails to explicitly teach that the disclosed brimonidine compound is at least two-fold to fifty-fold more selective (claim 1) or at least seven-fold to twelve-fold more selective (claim 34) for the alpha-2 adrenergic receptor as compared to clonidine, Burke et al. ("Preclinical Evaluation of

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Brimonidine”, *Survey of Ophthalmology*, 41(Supp.1), 1996; S9-S18) is cited for its factual teaching that brimonidine is known in the art to have a 7-fold to 12-fold greater selectivity for the alpha-2 adrenoreceptor as compared to clonidine (abstract). Accordingly, even though Gil et al. does not specifically disclose the degree of selectivity of brimonidine for the alpha-2 adrenoreceptor as compared to clonidine, Burke et al. provides the factual extrinsic evidence to show that this is a characteristic that is inherent in the teaching of the compound brimonidine.

Moreover, regarding Applicant’s limitation directed to topical administration of the active agent brimonidine tartrate, Wymenga et al. teaches the transdermal application of the alpha-adrenergic agonist to reduce the incidence of hot flushes in menopausal women. The teaching and suggestion of transdermal application of the alpha-adrenergic agonist is considered to meet Applicant’s limitation directed to topical administration because, as evidenced by Dictionary.com, transdermal is defined as “applied to the skin, usually as part of an adhesive patch for absorption into the bloodstream” and topical is defined as “of, pertaining to, or applied externally to a particular part of the body”. In view of such teachings, the fact that transdermal administration necessarily means application directly to the skin clearly meets the requirements of “topical” administration as instantly claimed, which is defined in the art as application externally to a particular part of the body (i.e., in this case, the skin organ). As a result, the teaching and suggestion to apply an alpha-adrenergic agonist transdermally to the skin clearly meets Applicant’s claimed limitation directed to topical administration of the same, since transdermal administration necessarily circumscribes external application directly to the skin, absent any factual evidence to the contrary.

It is clarified for the record that Applicant has failed to provide any explicit definition of the term “topically administering” in the instant specification so as to direct the interpretation of the term for examination. Accordingly, in the absence of a definition for the term “topically administering”, the Examiner defaults to the broadest, most reasonable interpretation of this term consistent with the art to the

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claims in accordance with the MPEP at §2111 and, therefore, relies upon the Dictionary.com reference as described *supra* for the art-accepted meaning of the term.

Note that cancellation of claims 5-6, 13, 18 and 26 renders the instant rejection **moot** as applied to such claims.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that Wymenga et al. discloses oral or transdermal administration of clonidine, which are allegedly forms of systemic administration, whereas the instant claims are directed to topical administration of the active agent. Applicant argues that topical administration differs from systemic administration in that a drug administered topically does not enter the bloodstream in a significant amount as compared to systemic administration, which does enter the bloodstream and is distributed throughout the body. Applicant additionally argues that Wymenga et al. only discloses the use of clonidine and fails to teach or suggest a selective alpha-2 adrenergic agonist (i.e., one that is at least two- to fifty-fold more selective for the alpha-2 adrenergic agonist as compared to clonidine). Still further, Applicant alleges that Gil et al. fails to disclose that brimonidine and clonidine are functionally equivalent and relies upon the reference to Burke et al. (citation *supra*) to show that the two compounds are not functionally equivalent because they differ in selectivity for the alpha-2 adrenoreceptor. Lastly, Applicant asserts that Gil et al. is directed to a method of alleviating pain, which is distinctly different than treating menopause-associated hot flashes, and does not teach or suggest the use of brimonidine for treating menopause-associated hot flashes.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Initially, it is noted that Applicant advances no specific reasons or evidence, aside from Counsel's own speculation, in support of the position that transdermal administration is a manner of systemic administration and differs from topical administration in the amount of active agent that is absorbed into

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the bloodstream. This assertion by Counsel is an unsupported allegation and fails to take the place of evidence in the record. Statements of this nature are clearly unpersuasive in accordance with the guidance provided at MPEP §2145, which states, “The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)”. Accordingly, there is no reason or basis advanced by Applicant to reasonably conclude that the teaching of transdermal administration does not meet Applicant’s claimed limitation directed to topical administration and, as a result, such an argument is unpersuasive in establishing nonobviousness of the claimed invention.

That being said, it is maintained herein that the transdermal manner of administration of the alpha-adrenergic agonist of Wymenga et al. meets Applicant's limitation directed to topical administration of the instantly claimed alpha-2 adrenergic agonist, brimonidine tartrate. It is first noted that Applicant has failed to specifically and explicitly define "topical" administration as instantly claimed as intending to circumscribe only those forms of topical administration wherein there is minimal absorption of the active agent into the bloodstream. Accordingly, the argument that “topical” administration as instantly claimed precludes transdermal administration wherein a greater amount of the active agent is absorbed into the bloodstream as disclosed by Wymenga et al. is unpersuasive because (1) neither the specification nor claims as originally filed expressly exclude such a manner of administration from the scope of the term “topical administration” and (2) Applicant has failed to point to any evidence supporting this alleged fundamental difference between topical and transdermal administration.

Furthermore, because Applicant has failed to provide any explicit definition of the term “topically administering” in the instant specification so as to direct the interpretation of the term for examination, the Examiner defaults to the broadest, most reasonable interpretation of this term consistent with the art to the claims in accordance with the MPEP at §2111. In support of this position, the Examiner relies upon the reference to Dictionary.com, which defines transdermal as “applied to the skin, usually as part of an

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adhesive patch for absorption into the bloodstream” and topical as “of, pertaining to, or applied externally to a particular part of the body”, for the art-accepted meaning of each term. In view of such teachings, the fact that transdermal administration as taught by the cited prior art necessarily circumscribes application directly to the skin clearly meets the requirements of “topical” administration as instantly claimed, which circumscribes application externally to a particular part of the body (i.e., in this case, the skin organ), absent any factual evidence to the contrary.

Secondly, Applicant’s argument that Wymenga et al. only discloses the use of clonidine and fails to teach or suggest a selective alpha-2 adrenergic agonist (i.e., one that is at least two- to fifty-fold more selective for the alpha-2 adrenergic agonist as compared to clonidine) is similarly unpersuasive. The motivation to substitute the alpha-adrenergic agonist clonidine with another known alpha-adrenergic agonist, such as, e.g., brimonidine tartrate, is not based upon alpha-2 adrenoreceptor selectivity, but rather is based upon the common and shared function of simply acting as an alpha-adrenergic agonist. In view of the fact that the two compounds clearly share this function as alpha-adrenergic agonists, the substitution of one compound for another would have reasonably yielded predictable results (i.e., in this case, an alpha-adrenergic agonist effect) to one of ordinary skill in the art at the time of the invention.

In other words, there is still a motivation, reason, teaching and/or suggestion to substitute the alpha-adrenergic agonist clonidine as disclosed by Wymenga et al. with the alpha-adrenergic agonist brimonidine tartrate as disclosed by Gil et al. on the grounds that the two compounds very clearly share a common function of agonizing alpha-adrenoreceptors and Wymenga et al. provides a clear teaching that menopause-associated hot flashes may be reduced in patients experiencing such a condition using a compound that has (non-specific) alpha-adrenergic agonist activity, such as clonidine. Accordingly, the fact that Wymenga et al. fails to teach that the compound must have selectivity for the alpha-2 adrenoreceptor that is greater than that of clonidine is immaterial to the present conclusion of obviousness because Wymenga et al. clearly implicates the agonism of alpha-adrenoreceptors as an effective means of

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reducing menopause-associated hot flashes without regard to the degree of selectivity the compound has for the alpha-1 receptor versus the alpha-2 receptor or as compared to other agonists. So long as the compound has alpha-adrenergic agonist activity as disclosed by Wymenga et al., the cited prior art clearly supports the *prima facie* obviousness of using brimonidine tartrate in place of clonidine on the grounds that the substitution of one known element for another known element, wherein both function in the same manner, would yield a predictable result (again, in this case, alpha-adrenergic agonism) and, therefore, would have provided a reasonable expectation of successfully accomplishing the claimed therapeutic objective.

Thirdly, the basis of Applicant's allegation that Gil et al. fails to disclose that brimonidine and clonidine are functionally equivalent is unclear. Gil et al. specifically, expressly and unequivocally discloses brimonidine and clonidine each as compounds that function as alpha-adrenergic agonists. This is a clear and explicit acknowledgement in the prior art at the time of the instant invention that the two compounds shared the same overall function as alpha-adrenergic agonists and, thus, are "functionally equivalent". The very fact that the two compounds may exhibit differing *selectivity* for the alpha-2 adrenoreceptor does not negate this clear teaching that the two compounds fundamentally act as agonists of alpha-adrenoreceptors. In fact, one of ordinary skill in the art would have reasonably expected that the degree of selectivity would have differed between the two compounds due to the chemical and structural differences between the two compounds. Accordingly, Applicant's allegation that clonidine and brimonidine are not functionally equivalent to one another on the grounds that they do not share identical selectivity for the alpha-adrenoreceptor is unpersuasive because, while the degree of selectivity may differ between the two compounds, the fact remains that Wymenga et al. clearly teaches the efficacy in agonizing the alpha-adrenoreceptor to reduce the incidence of menopause-associated hot flashes and, therefore, also clearly suggests that the use of another compound with the same function in agonizing alpha-adrenoreceptors (i.e., in this case, brimonidine tartrate as disclosed by Gil et al.) would have been

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reasonably expected to achieve this same therapeutic effect as the clonidine compound used in Wymenga et al.

Fourthly, in response to Applicant's argument that the reference to Gil et al. discloses methods of alleviating pain and fails to teach or suggest the treatment of cutaneous facial flushing caused by menopause-associated hot flashes, such remarks are directed toward the individual teachings of the cited reference without considering the reference *as it was combined* with Wymenga et al. As a result, focusing solely on the discrete teachings of this cited reference is tantamount to examining it inside of a vacuum and fails to be persuasive in establishing non-obviousness because it is the *combined* teachings that are the basis for a proper conclusion of obviousness, not each individual reference alone. In other words, it must be remembered that the references are relied upon in combination and are not meant to be considered separately. To properly conclude obviousness of an invention *does not require the claimed invention to be expressly suggested in its entirety by any one single reference under 35 U.S.C. 103(a)*. Rather, the test is *what the combined teachings* of the references would have suggested to those of ordinary skill in the art. Please reference *In re Young*, 403 F.2d 754, 159 USPQ 725 (CCPA 1968) and *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Furthermore, it is noted that the reliance upon Gil et al. was not made to bodily incorporate the features of the reference into Wymenga et al. Rather, it was relied upon for its teaching of other functionally equivalent alpha-adrenergic agonist compounds that were known in the art at the time of the invention and would have been reasonably substituted for the clonidine compound disclosed by Wymenga et al. for the predictable result of agonizing the alpha-adrenergic receptors. The fact that Gil et al. discloses the use of such alpha-adrenergic agonists for alleviating pain does not negate the teaching that clonidine, brimonidine, tizanidine, etc. are each compounds that function similarly as alpha-adrenergic agonists. Accordingly, in view of such a teaching of Gil et al., it remains that the use of other functionally equivalent alpha-adrenergic agonists (i.e., in the instant case, the use of brimonidine rather

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than clonidine as disclosed by Wymenga et al.) would have naturally commended itself, and would have been *prima facie* obvious, to one of ordinary skill in the art at the time of the invention because (1) the prior art was sufficiently well developed at the time of the present invention such that it clearly recognized the functional equivalency of compounds such as clonidine and brimonidine as alpha-adrenergic agonists, as evidenced by Gil et al. and (2) the use of an alpha-adrenergic agonist compound was known in the art to reduce the incidence of menopause-associated hot flashes that result in cutaneous facial flushing, as evidenced by Wymenga et al., and, thus, suggests that other alpha-adrenergic agonist compounds could be used with a reasonable expectation of success in reducing the incidence of the same, absent factual evidence to the contrary.

For these reasons set forth *supra*, and those previously made of record at pages 12-15 of the Office Action dated August 21, 2007, rejection of claims 1-2, 11-12 and 34-36 is proper.

Conclusion

Rejection of claims 1-2, 11-12 and 34-36 is proper.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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/Leslie A. Royds/
Patent Examiner, Art Unit 1614

June 4, 2008

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614